REMARKS

Claims 2, 39, 42, 45, 48, 51, 54, 57, 60, 63, 66, 69, 72, 75, 78, 81, 84, 87, 90, 93, 96, 99 and 102 were pending in this application. According to the September 19, 2001 Office Action, claims 2, 39, 42, 45, 48, 51, 54, 57, 60, 63, 66, 69, 72, 75, 78, 81, 84, 87, 90, 93, 96, 99 and 102 finally rejected. Accordingly, claims 2, 39, 42, 45, 48, 51, 54, 57, 60, 63, 66, 69, 72, 75, 78, 81, 84, 87, 90, 93, 96, 99 and 102 are under consideration.

Rejection under 35 U.S.C. §103(a)

The Examiner rejected claims 2, 39, 42, 45, 48, 51, 54, 57, 60, 63, 66, 69, 72, 75, 78, 81, 84, 87, 90, 93, 96, 99 and 102 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Ben-David et al. and Kelly in view Wojtacki et al., Sharma et al. and Labrie et al. for reasons set forth in the prior Office Action.

In response, Applicant respectfully traverses the Examiner's rejection. As indicated previously, Applicant throughout the specification has demonstrated the unexpected and synergistic effects of the combination of SERMs and sex steroid precursors on the treatment of the reduction of the risk of acquiring hypercholesterolemia. In addition, Applicant also submitted a Declaration under Rule 132 showing that a real beneficial effect is obtained by the combination of DHEA and EM-652.HCl on total cholesterol serum levels. A decrease of 73.6% of the total cholesterol concentration (0.65±0.06 mmol/L) is obtained with the combination while this decrease is only of 64.6% (0.87±0.04 mmol/L) or 35.4% (1.59±0.10 mmol/L) with EM-652.HCl or DHEA alone. The addition of DHEA to EM-652.HCl treatment allows for a significant additional reduction of 9% of the cholesterol serum levels.

However, the Examiner's position is that the evidence provided as unexpected and synergistic is not commensurate in scope with the claims. The Examiner objected that the claims have no limitation about the ratio of EM-1538 and the sex steroid precursor since they encompass any combination of the two ingredients, including a combination that is without a synergistic effect.

In reply, Applicant points out that with regard to the combination of EM-1538 (EM-652.HCl) and a sex steroid precursor, the ratio of the two drugs is not critical and the Examiner did not provide any reason to the contrary.

Preferably, both drugs are used at their optimal dose. Optimal doses for each component are very well described in the specification. The optimal doses of DHEA are defined as follows: "The blood level of DHEA is the final criteria of adequate dosage which takes into account individual variation in absorption and metabolism;" (see specification on page 34, lines 24-26), and "[t]reatment in accordance with the invention is suitable for indefinite continuation. It is expected that DHEA and/or 5-diol treatment will simply maintain DHEA levels within a range similar to that which occurs naturally in women before menopause (serum concentration between 4 and 10 micrograms per liter), or naturally in young adult men (serum concentration between 4 and 10 micrograms per liter)." (See specification on page 35, second paragraph).

The optimal doses of SERMs are defined as follows:

"Any SERM used as required for efficacy, as recommended by the manufacturer, can be used. Appropriate dosages are known in the art. Any other non steroidal antiestrogen commercially available can be used according to the invention. Any compound having activity similar to SERMs (example: Raloxifene) can be used. (See specification on page 39, last full paragraph).

SERMs administered in accordance with the invention are preferably administered in a dosage range between 0.01 and 10 mg/kg of body weight per day (preferably 0.05 to 1.0 mg/kg), with 5 mg per day, especially 10 mg per day, in two equally divided doses being preferred for a person of average body weight when orally administered, or in a dosage range between 0.003 to 3.0 mg/kg of body weight per day (preferably 0.015 to 0.3 mg/ml), with 1.5 mg per day, especially 3.0 mg per day, in two equally divided doses being preferred for a person of average body weight when parentally administered (i.e. intramuscular, subcutaneous or percutaneous administration)." (See specification on pages 39 and 40, bridging paragraph).

Applicant point out that optimal doses can vary depending on the individual being treated. The specification on page 34, line 28 to page 35, line 6 indicates that the attending

clinician will, especially at the beginning of treatment, monitor an individual patient's overall response and serum levels of sex steroid precursors, and monitor the patient's overall response to treatment, adjusting dosages as necessary depending on a given patient's metabolism or reaction to treatment. Accordingly, limitations on the amounts of the two ingredients is inappropriate as amounts used in treatments will vary depending on the individual being treated. As noted here, the specification provides ample guidance as to what parameters to look for in choosing particular doses for sex steroid precursors and SERMs. Given that and the fact that the specification as well as the previously submitted Declaration show the unexpected results with the combination treatment, the Examiner is kindly requested to withdraw this rejection.

In light of the foregoing, it is respectfully submitted that this application is now in condition to be allowed and the early issuance of a Notice of Allowance is respectfully solicited. If there are any issues or amendments the Examiner wishes to discuss, the Examiner is encouraged to contact the undersigned.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231, on March 19, 2002:

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Respectfully submitted,

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